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Recent Advances in Niosomal Drug Delivery: A Review

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Abstract

The production of niosomes, which are non-ionic surfactant vessels, involves hydrating synthetic non-ionic surfactants, either with or without the addition of cholesterol or another lipid. Due to their distinctive qualities, including biodegradability, biocompatibility, chemical stability, low production cost, ease of storage and handling, and low toxicity, non-ionic surfactant vesicles also known as niosomes have received a lot of attention in the field of modern drug delivery system. Niosomes are hydrated vesicular systems with a lamellar bilayer structure made of non-ionic surfactants with or without cholesterol, and they have a wide spectrum of solubilities that allow them to encapsulate a variety of bioactive chemicals. Niosomes have been tested as a delivery system for a variety of anti-cancer medications, genes, antigens, and other bioactive substances. This article focuses on recent developments in niosomal drug delivery, possible benefits over alternative delivery mechanisms, formulation techniques, characterisation techniques, and ongoing niosome research.

Keywords: Niosomes, Non-ionic surfactant, cholesterol, Drug delivery system.

Introduction

Niosomes arevesicle. Niosomes get their name from the fact that the vesicle is made up of a bilayer of non-ionic surface-active substances. The niosomes are miniscule in size and incredibly tiny. They are on the nanometre scale in size. They are structurally related to liposomes but differ in a number of ways. Increased research into these structures may result in new medication delivery strategies because niosomes have recently been proven to significantly improve transdermal drug delivery and can also be used for targeted drug a cutting-edge drug delivery technology that encapsulates the medication. [1,2]

They are vesicular systems that resemble liposomes and can transport both amphiphilic and lipophilic medications.Niosomes are created when non-ionic surfactant dry film is hydrated, which causes the hydrating solution to be ingested or encapsulated. In contrast to liposomes, which are more prone to oxidation, high cost, and the challenge of obtaining high purity levels that affect size and vesicular stability, niosomes are mostly composed of non-ionic surfactants, giving them the advantage of being more stable. Both hydrophilic and lipophilic medicines can be trapped by niosomes in the aqueous layer and vesicular membrane, respectively.

This review's objective is to outline the foundations of niosome creation, characterisation, and drug administration, paying particular focus to more recent findings. Niosomes are becoming more and more popular in the realm of drug delivery, and this article will give an overview of that interest.[3,4]

STRUCTURE OF NIOSOMES:

Niosomes is a bilayered, spherical structure made of cholesterol and nonionic surfactant, with the hydrophobic end of the nonionic surfactant facing inwards (toward the lipophilic phase). The closed lipid bilayer that envelops solutes in the aqueous phase, which resembles the outer and inner surfaces of the hydrophilic area and sandwiched the lipophilic area in between, is created when the hydrophilic end faces outwards (toward the aqueous phase). These non-ionic surfactant-based vesicles, or "niosomes," are thought to be either a less expensive non-biological alternative to liposomes or possibly a drug delivery system that, in vivo, resembles liposomes but has particular properties to achieve different drug distribution and release characteristics.[5,6]

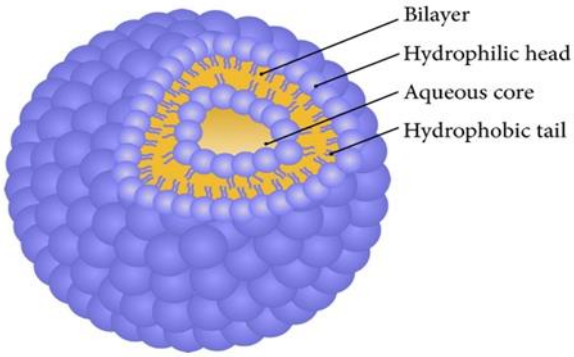

Figure 1: Structure of Niosomes

COMPOSITION OF NIOSOMES:-

Niosome preparation involves the employment of two components[7]

- Non-ionic surfactant
- cholesterol

A. Cholesterol, a steroid derivative, aids in giving niosomes their appropriate shape and solid structure.
B. Niosomes are prepared using non-ionic surfactants.

TYPES OF NIOSOMES:-

The classification of niosomes is based on the size, size of the bilayers, and manufacturing method. The many niosome kinds are described in the paragraphs that follow.[8,9,10]

- Multi lamellar vesicles (MLV)
- Large unilamellar vesicles (LUV)
- Small unilamellar vesicles (SUV)

A. Multi lamellar vesicles(MLV):These vesicles range from 0.5 to 10 metres in diameter. Multilamellar vesicles are the most prevalent type of niosomes. It is simple to make and, after

being stored for a while, mechanically stable. The use of these vesicles as a lipophilic compound is suitable medicine transporters**.**

B. Large unilamellar vesicles (luv): Due to the high ratio of aqueous to lipid compartments in these niosomes, membrane lipids can be used to efficiently entrap greater volumes of bioactive substances.

C. Small unilamellar vesicles (suv):These SUVs are mostly made of multilamellar vesicles thanks to electrostatic precipitation, the French press extrusion method, and sonication.

MECHANISM OF ACTION OF NIOSOMES AS PERMEATION ENHANCER:-

Niosomes' ability to increase drug transfer through the skin has been attributed to a number of different mechanisms, including the alteration of the stratum corneum's barrier function as a result of reversible perturbation of lipid organisation, reduction of transepidermal water loss, which increases the stratum corneum's hydration and loosens its tightly packed cellular structure, and adsorption and/or fusion of niosomes. Three routes—intercellular, transcellular (paracellular), and transappendageal—can be used for drug transport across the stratum corneum, which is primarily a passive process. After it has travelled through the epidermis, a substance could be eliminated by thedeeper tissues may go through the dermal circulation.The effectiveness of various tactics has been evaluated toenhance the stratum corneum's barrier function of drug penetration of the skin. Penetration improvement in particular one or more of the following three mechanisms could be used by ers to act. Niosomes can lengthen the period that a medication stays in the SC and epidermis when given topically they are believed to enhance the smoothness and characteristics of the horny layer by restoring lost skin lipid and minimising transepidermal water loss. [11,12,13]

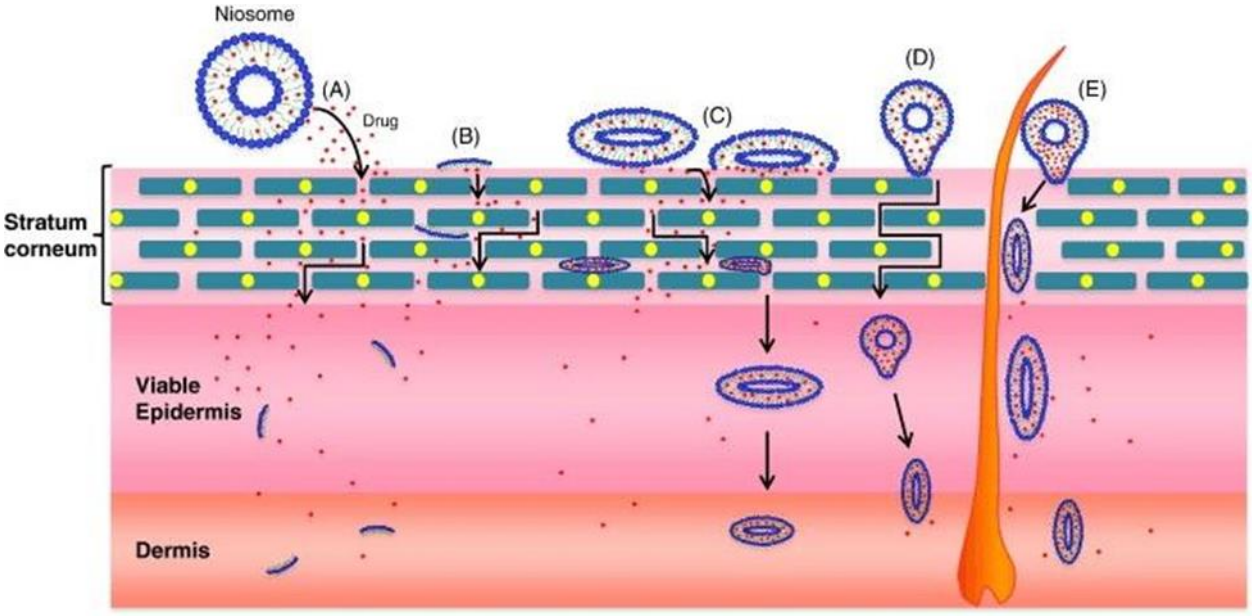

Figure 2:- Niosomes acts as skin permeation enhancer

ADVANTAGES OF NIOSOMES:-

- Due to the amphiphilic structure of niosomes, a variety of pharmacological compounds can be soluble in them.

- When compared to oily dose forms, the water-based vesicle suspension delivers great patient compliance.
- The infrastructure of hydrophilic, lipophilic, and amphiphilic in niosomes allows for the accommodation of drug molecules with a wide spectrum of solubilities.
- By adjusting the composition of the vesicle, size lamellarity, surface charge, tapping volume, and concentration, vesicle properties can be changed.
- They have the ability to release the medicine gradually and deliberately.
- Because of the chemical stability of their structural makeup, surfactants can be stored and handled without the need for special conditions like low temperature and inert gas.
- They may function as depot formulations, allowing for regulated medication release.
- They increase the oral bioavailability of medications that aren't very soluble.
- They can protect the drug from enzyme metabolism.
- Extremely cost-effective for large-scale production.
- They are safe and made of non-toxic, biocompatible, and biodegradable materials.
- Niosomes guard the medication against enzymatic deterioration.
- They can be administered orally, parentally, topically, or transdermally.
- It may shield the medication from enzyme metabolism. [14,15,16]

DISADVANTAGES OF NIOSOMES:-

- Physical unsteadiness.
- The encapsulated medicine may have a possibility to silt, aggregate, fuse, or leak during storage due to the niosomes' dispersion shape.
- Drugs in capsules hydrolyzing, reducing the shelf-life of the dispersion.
- Time taken process. [15,16]

METHOD OF PREPARATION:-

Thin-Film Hydration Method (TFH):- A quick and popular method of preparation is thin-film hydration. In this procedure, an organic solvent is used to dissolve surfactants, cholesterol, and various additives like charged molecules in a round-bottomed flask. The organic solvent is then eliminated using a rotary vacuum evaporator to produce a thin coating on the flask's interior wall. The dry film is hydrated above the surfactant's transition temperature (Tc) for a predetermined amount of time while being continuously shaken. By using this technique, multilamellar niosomes are created. [17,18]

Ether Injection Method (EIM):-In the ether injection method, the surfactants and additives are dissolved in diethyl ether and slowly injected through a needle into a constant-temperature aqueous drug solution that is above the boiling point of the organic solvent. A rotary evaporator is worn to withdrawal the organic solvent. Single-layered vesicles are formed during the vaporisation process. [19]

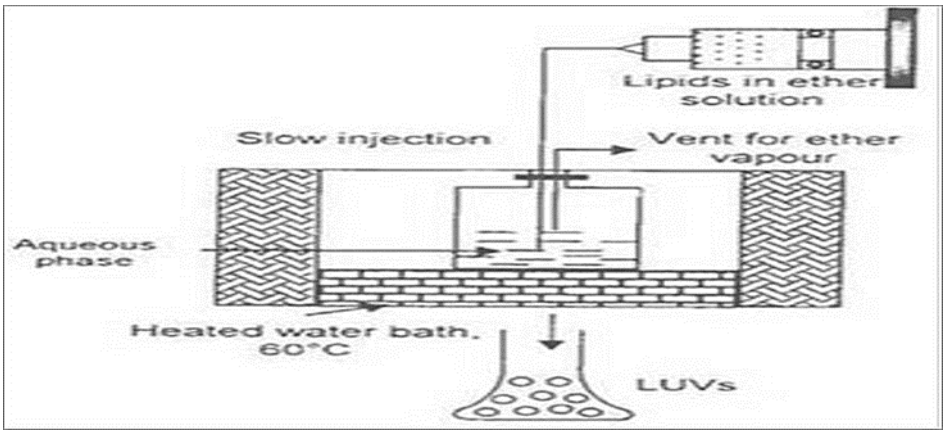

Figure 3: Ether injection method

Microfluidization Method:-The submerged jet idea is the foundation of the microfluidization process. In this technique, the fluidized streams of drug and surfactant interact at extremely high speeds in narrowly defined microchannels inside the interaction chamber. Niosomes are formed as a result of the energy and high speed impact. In the creation of niosomes, this approach provides more uniformity, smaller size, unilamellar vesicles, and good reproducibility. [20]

Proniosome:- Using the proniosomes technique, a surfactant-coated water-soluble carrier, such as sorbitol or mannitol, is used. A dry formulation is created as a result of the coating process. This substance is known as "Proniosomes," and it must be hydrated before usage. The inclusion of the aqueous phase results in the formation of the niosomes. This approach offers convenience in dosing, distribution, transportation, and storage and reduces physical stability issues including the aggregation, leakage, and fusing problem while producing better outcomes than traditional niosomes. [21]

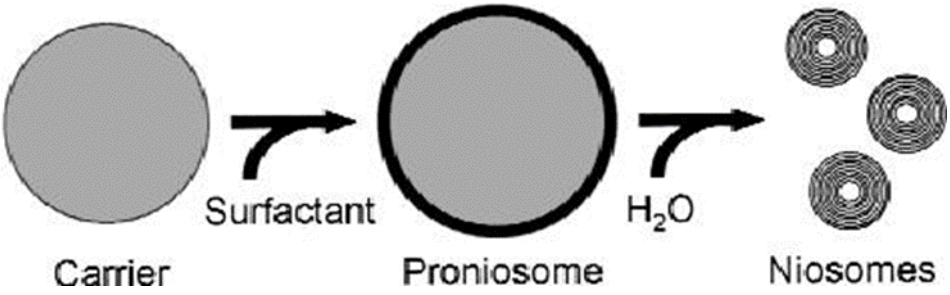

Figure 4: Proniosome

Heating Method:- Mozafari et al. developed this unique procedure. Separately hydrating the surfactants and the cholesterol in the buffer, the mixture is then heated to 120°C while being stirred to dissolve the cholesterol. After lowering the temperature, stirring continues while surfactants and other chemicals are added to the buffer in which cholesterol has been dissolved. As they form, niosomes are held at ambient temperature for a short period of time before being stored at 4-5°C under a nitrogen environment until needed. [22]

The "Bubble" Method:- In this technique, a glass flask with three necks is filled with surfactants, additives, and the buffer. Niosome components are combined using a homogenizer after being dispersed at 70°C. The flask is then placed in a water bath and nitrogen gas is bubbled at a temperature of 70 °C. A sample

of homogenised surfactants is exposed to nitrogen gas, which causes the development of large unilamellar vesicles. [23]

CHARACTERIZATION OF NIOSOMES:-

For the clinical uses, niosome characterisation is crucial. Niosome stability and in vivo performance are both significantly influenced by characterization factors. Thus, it is necessary to analyse various factors, including shape, size, polydispersity index (PI), number of lamellae, zeta potential, encapsulation effectiveness, and stability. [24,25,26]

Size and Morphology:-scanning electron microscopy (SEM), dynamic light scattering (DLS), and transmission The most popular techniques for determining niosome sizes and morphology are electron microscopy (TEM), freeze fracture replication electron microscopy (FF-TEM), and cryotransmission electron microscopy (cryo-TEM). DLS concurrently gives useful data on the homogeneity of the solution and cumulative information on particle size. A single population of scatterers is implied by a single sharp peak in the DLS profile. In this regard, the PI is beneficial. The morphology of the niosomes is typically studied using microscopic methods.

S*tability*:- By measuring the mean vesicle size, size distribution, and entrapment effectiveness over multiple month storage periods at various temperatures, it is possible to assess the stability of niosomes. Niosomes are sampled regularly throughout storage to determine how much of the drug is retained in them. This percentage is then analysed using UV spectroscopy or HPLC techniques.

Entrapment Efficiency:- The percentage of a drug that is captured and extracted by niosomes is known as entrapment efficiency (EE%). Centrifugation, dialysis, or gel chromatography are methods that can be used to extract unencapsulated free medication from the niosomal solution. By destroying the vesicles after this phase, the loaded medicine can be released from the niosomes.

Zeta Potential :-Zetasizer and DLS equipment can be used to measure the surface zeta potential of niosomes. The behaviour of niosomes is significantly influenced by their surface charge. Charged niosomes are typically more resistant to aggregation than are uncharged vesicles. Niosomes that had been loaded with paclitaxel were made by Bayindir and Yuksel, who also looked into their physicochemical characteristics such zeta potential.

APPLICATION OF NIOSOMES:-

Niosomes as Drug Carriers :- Iobitridol, a diagnostic substance used for X-ray imaging, has also been transported by niosomes. Topical niosomes can work as a solubilization matrix, a local depot for the prolonged release of substances with dermal activity, penetration enhancers, or a membrane barrier that limits the pace at which medications are absorbed into the body.

*Drug Targetting:-*Drug targeting is one of the most advantageous properties of niosomes. To target medications to the reticuloendothelial system, niosomes can be employed. The reticulo-endothelial system (RES) takes up niosome vesicles preferentially. Circulating serum variables regulate how much of niosomes are taken up call them opsonise. The niosome is marked by these opsonise for removal. The use of such medication localization is made toAny tumours that have a history of spreading to the spleen and liver should be treated. Drugs can also be localised in this way and applied in the treatment of liver parasite infections. Drugs can be targeted with niosomes, according to Not the RES, but other organs. Niosomes can be connected to a carrier system (such an antibody) in a variety of ways. The lipid surface of the niosome is easily bound by immunoglobulins to target

*Delivery of Peptide Drugs :-*It has long been difficult to avoid the enzymes that would break down peptides used in oral medication administration. It is being researched if niosomes may successfully shield peptides from gastrointestinal peptide degradation. An in vitro investigation using oral administration of a vasopressin derivative trapped in niosomes revealed that drug entrapment dramatically improved the peptide's stability.

*Niosomes as Carriers for Haemoglobin:-*Haemoglobin can be carried through the blood by niosomes. In anaemic patients, the niosomal vesicle, which is permeable to oxygen, can serve as a carrier for haemoglobin.

Leishmaniasis:- A parasite from the genus Leishmania infects the liver and spleen cells to cause leishmaniasis, a disease. When treating illnesses where the infectious agent is found in a reticuloendothelial system organ, niosomes can be employed to target the medicine (RES). Antimonials, which are routinely prescribed medications and are related to arsenic, harm the heart, liver, and kidney at high concentrations. According to reports, two dosages administered on consecutive days had an additive impact and improved the niosomal formulation's ability to dissolve sodium stibogluconate. [27,28]

RECENT ADVANCES: -

Recent studies on transdermal drug delivery from niosomes in various disease models have been conducted, and current research efforts are concentrated on process optimization, novel compositions, and final formulations.Since edge activators (such as ethanol) give vesicles their elastic properties, allowing them to more easily penetrate into the deeper layers of the skin, new highly flexible niosomes, known as elastic vesicles, have prefer and are describe to be effectual at transport molecules through the skin. The liquid form of the preparation is another key drawback of niosomes since when administered, they may leak from the application site.By including niosomes in a suitable medium, which is accomplished by adding gelling agents to niosomal dispersions to create a niosomal gel, this difficulty can be overcome. Niosomal gels were discovered to improve the skin's ability to retain medicines and to give highand continued drug levels in the skin. Proniosomes, also known as "dry niosomes," which have been proposedas niosomal formulations, are another step in the evolution of niosomes. These formulations must be hydrated before use, which creates an aqueous niosomal dispersion. Because they are hydrated with water from the skin under occlusion when applied to the skin, proniosomes reduce the aggregation, leakage, and fusion issues related to conventional niosomes and provide a flexible transdermal drug delivery system. A summary of research results on transdermal niosomal drug delivery systems conducted over the previous seven years.

Specific study teams have created niosomes that contain NSAIDs (nonsteroidal anti-inflammatory drugs). After being taken orally, these medications may irritate the local mucosa and go through first-pass metabolism in the liver, which results in partial inactivation. As a result, only 50% of the medication enters the bloodstream. For prolonged usage of this medication, especially when used to treat rheumatic symptoms, topical dose formulations are preferred. The ability of topical NSAIDs to enter the skin plays a key role in their effectiveness.ElMaghraby et al54 looked at the impact of adding skin penetration boosters to proniosomes on the system's capacity to deliver pharmaceuticals transdermally. Nisoldipine, a second-generation dihydropyridine calcium antagonist, was chosen as the model medicine to accomplish this goal due to the fact that it has a low and variable bioavailability after oral administration due to substantial first-pass liver degradation. In order to boost the transdermal administration of nisoldipine

from this provesicular system and to develop a new way for doing so, lecithin, oleic acid, and propylene glycol were used as enhancers.

According to the published report, when compared to the saturated aqueous control formulation, all proniosomal formulations significantly increased the rate at which the drug was delivered through the skin, and the oleic acid/propylene glycol combination's enhancing efficacy was even greater than lecithin's. [29,30]

CONCLUSION:-

While niosome technology is still very young, it is already demonstrating promise in the treatment of cancer and infectious diseases. Several cosmetic items already employ the method. Niosomes are a promising drug delivery technology that can be used for a variety of drug delivery methods, including targeting, ophthalmic, topical, parenteral, etc. However, much more research is needed to fully realise the potential of this cutting-edge drug delivery system.Niosomal carriers are safer than ionic drug carriers, which are more toxic and inappropriate. Additionally, there are no additional requirements for handling or storing niosomes. Niosomes, which are vesicular drug delivery systems, can be delivered by macrophages, which are known to colonise tumour cells.It might be able to use the activated macrophage system to deliver the anti-tumor chemicals in the vesicles to tumour locations more quantitatively. Only animal testing of this targeted drug delivery system has been documented thus far, but additional clinical studies in human volunteers as well as pharmacological and toxicological research in both animals and humans may help to fully utilise niosomes as effective drug carriers for treating conditions like cancer, infection, and AIDS, among others. There is a lot of potential for hazardous anti-cancer, anti-infective, anti-inflammatory, anti-viral, and other medications to be encapsulated in niosomes.

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